

## PATENT COOPERATION TREATY

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From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

To:

ASTRAZENECA  
Global Intellectual Property  
Mereside, Alderley Park  
Macclesfield  
Cheshire SK10 4TG  
GRANDE BRETAGNE

CODE	DATE	NTD
ANKOM	26 NOV 2004	GIPS
DATA ENTERED		Date of mailing (day/month/year)
FINAL CHECK		

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT

(PCT Rule 71.1)

Applicant's or agent's file reference  
100756-1 WO

## IMPORTANT NOTIFICATION

International application No.  
PCT/GB 03/02959International filing date (day/month/year)  
09.07.2003Priority date (day/month/year)  
13.07.2002Applicant  
ASTRAZENECA AB

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

## 4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions are patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international  
preliminary examining authority:

European Patent Office  
D-80298 Munich  
Tel. +49 89 2399 - 0 Tx: 523656 epmu d  
Fax: +49 89 2399 - 4465

Authorized Officer

Siefert, A

Tel. +49 89 2399-2469



# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT (PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>100756-1 WO</b>	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)																
International application No. <b>PCT/GB 03/02959</b>	International filing date (day/month/year) <b>09.07.2003</b>	Priority date (day/month/year) <b>18.07.2002</b>															
International Patent Classification (IPC) or both national classification and IPC <b>A61K31/445</b>		<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 33%;">CODE</th> <th style="width: 33%;">DATE</th> <th style="width: 33%;">NTD</th> </tr> </thead> <tbody> <tr> <td> </td> <td> </td> <td> </td> </tr> <tr> <td colspan="3"> <b>ANKOM 26 NOV 2004 GIPS</b> </td> </tr> <tr> <td colspan="3"> <b>DATA ENTERED</b> </td> </tr> <tr> <td colspan="3"> <b>FINAL CHECK</b> </td> </tr> </tbody> </table>	CODE	DATE	NTD				<b>ANKOM 26 NOV 2004 GIPS</b>			<b>DATA ENTERED</b>			<b>FINAL CHECK</b>		
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Applicant <b>ASTRAZENECA AB</b>																	
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of    sheets.</p>																	
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li>I    <input checked="" type="checkbox"/> Basis of the opinion</li> <li>II   <input type="checkbox"/> Priority</li> <li>III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li> <li>IV   <input type="checkbox"/> Lack of unity of invention</li> <li>V    <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability citations and explanations supporting such statement</li> <li>VI   <input type="checkbox"/> Certain documents cited</li> <li>VII <input type="checkbox"/> Certain defects in the international application</li> <li>VIII <input type="checkbox"/> Certain observations on the international application</li> </ul>																	
Date of submission of the demand  <b>20.01.2004</b>	Date of completion of this report  <b>23.11.2004</b>																
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer  <b>Gavriliu, D</b>  Telephone No. +49 89 2399-8274																



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. **PCT/GB 03/02959**

**1. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, Pages**

1-80 as originally filed

**Claims, Numbers**

1-13 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority in written form.  
☐ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to report.)*

6. Additional observations, if necessary:

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**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,  
☒ claims Nos. 11 (with respect to industrial applicability)

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):  
☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):  
☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.  
☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the Standard.  
☐ the computer readable form has not been furnished or does not comply with the Standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-10,12-13
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-10,12-13
Industrial applicability (IA)	Yes: Claims	1-10,12-13
	No: Claims	

2. Citations and explanations

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB 03/02959

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claims 11 relates to subject-matter considered by this Authority to be covered by the provision of Rule 67.1(iv)PCT. Consequently, no opinion will be formulated with respect to the novelty, inventive step and industrial applicability of the subject-matter of this claim(article 34(4)(a)(i)PCT).

**Re Item V**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Reference is made to the following documents:**

D1: WO-A-0012477  
D2: WO-A-0012478  
D3: WO-A-0044723  
D4: WO-A-9965867

**2. Novelty (Article 33(1) and 33(2)PCT):**

The subject-matter of the present application relates to N-sulfonylpiperidines, useful as inhibitors of metalloproteinase.

The present compounds differ from the compounds disclosed by D1 through the substituents R3 and R4 (none of them can be a benzyl moiety - see present Claim 1 and description-page 3-line 19-page 5-line 7 as well as example 6-D1) and from the compounds disclosed by D2 on account of the provisio (see present Claim 1 and example 14-D2). The compounds disclosed by D3 are double substituted on the position 4 of the piperidine ring (see examples D3 and the present Claim 1). The compounds disclosed by D4 differ from the present ones through the N-substituent of the piperidine ring. Consequently, the novelty of the present subject-matter is acknowledged.

**3. Inventive step (Article 33(1) and (3) PCT).**

The present application describes N-sulfonylpiperidines, bearing on the sulfonyl

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chain a  $-\text{CONOHR}^{15}$  or  $-\text{N}(\text{OH})\text{CHO}$  moiety and in position 4 a ring (B) linked through a X chain. The present compounds are useful in the manufacture of a medicament in the treatment of a disease condition mediated by one or more metalloproteinase enzymes.

D1, which is regarded as being the closest prior art, discloses N-sulfonyl-piperidines as metalloproteinase enzymes inhibitors. Example 6 (page 22-D1) differs only through the substituent benzyl (corresponding to the present R3) from the present compounds.

The technical problem underlying the present application is to be seen in a provision of further N-sulfonylpiperidine derivatives useful as metalloproteinase inhibitors.

Document D2 discloses 4-aryloxypiperidines as metalloproteinase agents. The compounds disclosed in example 14 of D2 (pages 50-51) differ from the present claimed compounds only on the account of the proviso (in the present case the ring B is linked on the piperidine ring through a  $-(\text{CR}^9\text{R}^{10})_t-\text{O}-(\text{CR}^{11}\text{R}^{12})_u-$  or  $-(\text{CR}^9\text{R}^{10})_t-\text{SO}_{0-2}-(\text{CR}^{11}\text{R}^{12})_u-$  chain, without the possibility that  $t+u=0$ , as in D2).

Documents D3-D4 disclose metalloproteinase inhibitors which contain a piperidine ring substituted in position 4 either with a (hetero)arylmethoxy moiety (D4-tables 8-13) or with an arylmethylene(sulfinyl or sulfonyl) moiety (D3-e.g. example 30-49).

Since, only very minor modifications of the compounds disclosed by D1-D2 are required in order to arrive at the claimed derivatives and moreover the substitution of the piperidine ring in position 4 with an arylmethoxy or arylmethylenesulfonyl moiety was already disclosed by D3-D4, the person skilled in the art would expect that the same qualitative effect would be maintained in such similar compounds.

The problem underlying the present application thus appears to lie in the provision of further N-sulfonylpiperidine derivatives possessing unexpected properties over the prior art.

An inventive step cannot therefore be acknowledged, in the absence of comparative data showing that substantially all the claimed compounds have an unexpected property or improved activity with respect to the structurally closest prior art compounds, which is attributable to the distinguishing feature of the

**INTERNATIONAL PRELIMINARY  
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International application No. PCT/GB 03/02959

invention.

Moreover the disclaimer of Claim 1 cannot be used to make a novel invention inventive, while the above-mentioned proviso excludes compounds from the same technical field and thereof it cannot be seen as "accidentally disclosure".

**4. Industrial applicability (Article 33(4)PCT).**

For the assessment of the present claim 11 on the question whether it is industrial applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may also allow, however, claims to a known compound for the manufacture of a medicament for a new medical treatment.